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Review

Impact of physical activity on health-related quality of life in osteoporotic and osteopenic postmenopausal women: A systematic review

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ABSTRACT

Objective: This meta-analysis included papers which evaluated the effects of physical activity on the health-related quality of life (HRQoL) of osteoporotic and osteopenic postmenopausal women.

Methods: Four English databases were searched for relevant randomized clinical trials (RTCs) published from 1970 to June, 2014. Eligible RCTs which used the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) as their outcome measure were selected for inclusion.

Results: Five RCTs were included in the final meta-analysis. The results showed that physical activity produced favorable effects in the HRQoL domains of physical function ($p = 0.001$) and pain ($p = 0.01$), but not in other domains. Compared with a single exercise, combined exercise produced more favorable effects on both physical function ($p = 0.0004$) and pain ($p = 0.02$). Short-term physical activity produced significant favorable results in all general health domains of HRQoL ($p = 0.01$), whereas middle-term physical activity produced significant improvements only in the physical function ($p < 0.01$) domains of HRQoL. Long-term physical activity produced significant improvement only in the pain domains of HRQoL ($p < 0.01$), and only in the physical activity group when compared with a control group.

Conclusion: Only weak evidence supports the notion that physical activity effectively improves the health-related quality of life of osteoporotic and osteopenic postmenopausal

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women. Compared with a single exercise, combined exercise produced favorable effects on both physical function and pain. However, different lengths of exercise produced improvements in different domains.

1. Introduction

As the most common skeletal disorder, postmenopausal osteoporosis (PMO) is caused by accelerated bone resorption and a systemic calcium imbalance resulting from estrogen deficiency induced by menopause [1,2]. Additionally, PMO can result from a pathological process that causes loss of bone mass and micro-architectural deterioration of bone tissue [2]. PMO most frequently presents with clinical symptoms which include loss of physical function accompanied by pain, deformity, and depression [3,4]. In 2005, it was estimated that PMO affected 10 million women world-wide, including 8 million in the United States [5]. Other than specific back pain, the early symptoms of osteoporosis are rarely reported; and thus osteoporosis is rarely diagnosed prior to an initial bone fracture [6].

Until now, osteoporosis has mainly been treated by cautioning the patient to avoid fractures and prescribing various pharmaceutical agents. Currently, calcitonin, bisphosphonates, raloxifene, parathyroid hormone, and denosumab, are approved for treatment of postmenopausal osteoporosis in the United States [7]; however, the optimal duration for taking such agents remains unknown, because the risk benefit ratio associated with of long-term pharmacologic treatment of osteoporosis is unclear [7]. Moreover, the most impressive drugs may be too expensive for purchase by clients and patients in developing countries. Hence, when treating osteoporosis, non-pharmacologic therapies provide a promising and suitable alternative to prescription drugs. Current guidelines for treating osteopenia include a recommendation for physical activity [8]. Moreover, the results of several studies have indicated that regular physical exercise can help to reduce pain in postmenopausal women, reduce the incidence of falls and fall-related injuries, and improve postural stability and mobility [9–12]. However, only a few studies have specifically focused on the efficacy of exercise for increasing the HRQoL of postmenopausal women with low bone mass.

HRQoL is a subset of overall life quality, and includes domains of physical, emotional, and social well-being [13]. As recognized by WHO in 2003, the presence of osteoporosis accompanied by a fracture significantly impairs an individual's HRQoL by greatly reducing physical functioning while producing pain, social isolation, and depression [14]. Thus HRQoL is an important outcome that should be considered when planning physical therapy regimens for osteoporosis patients. A meta-analysis published in 2009 summarized and critically evaluated the effects of exercise on HRQoL in postmenopausal women with low bone mass, and the studies included in that analysis utilized either the Short Form 36 (SF-36) questionnaire or Quality of Life of the European Foundation for Osteoporosis (QUALEFFO) questionnaire to gather data [15]. Two of the RCTs included in that meta-analysis gathered their quality of life data by administering the generic health-related SF-36 questionnaire [15]; however, the use of such generic instruments can harm the validity of results [13,16]. Our meta-analysis, only included RCTs which used a disease-specific questionnaire to examine the effects of physical activity on the quality of life of postmenopausal women with osteoporosis or osteopenia, and these studies included some recent RCTs with results published after August, 2009.

2. Materials and methods

This study was conducted according to guidelines described in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [17].

2.1. *Search strategies*

The English databases Medline, Embase, CINAHL, and the Cochrane Central Register of Controlled Trials were searched for relevant clinical studies which had their results published between 1970 and June, 2014. The search strategies utilized are shown in Appendix A. Next, review articles were searched and a snowball search was conducted.

2.2. *Selection criteria*

Only peer-reviewed reports describing the results of randomized controlled trials (RCTs) were deemed eligible for inclusion in our meta-analysis; however, trial results published in the form of a dissertation were also considered as potential candidates. All included studies were required to satisfy the following criteria:

P (population): The RCT studied postmenopausal women with low bone mass, as diagnosed using WHO criteria for osteoporosis and osteopenia.

I (intervention): In addition to single-muscle strength training, both modern and traditional physical therapy regimens, as well as programs that used Tai Chi (TC) or yoga were included in our systematic review.

C (comparison): Studies with both real exercise activities and sham exercises were included in the systematic review.

O (outcome): All included studies used the European Foundation for Osteoporosis (QUALEFFO) questionnaire and its five domains (physical function, pain, general health, social function, and mental health) as a specific instrument to measure the effects of physical activity on the HRQoL of postmenopausal women with low bone mass. The score for each domain was provided on a scale ranging from 0 to 100, with lower scores indicating a better HRQoL [18,19].

2.3. *Data extraction, quality and validation*

The complete text of each included article was read by two independent reviewers (Xu and Ji) who extracted relevant data based on the predetermined criteria. The Cochrane risk of bias tool was used to evaluate the methodological quality of each included trial [20], and each RCT was assessed for the following characteristics: (i) selection bias; (ii) performance bias; (iii) detection bias; (iv) attrition bias; (v) reporting bias. The terms 'Low', 'Unclear', and 'High' referred to low, uncertain, and high risks of bias, respectively. In most cases, disagreements were resolved by discussion between the two reviewers. If disagreement remained after discussion, a third reviewer (Lu) was consulted and made the final decision.

2.4. *Quantitative data synthesis*

The meta-analysis was performed using RevMan 5.2 software (Cochrane Collaboration, Oxford, UK, available from the website for free: http://www.ccims.net/revman/download). The mean values and standard deviations (SDs) for changes which occurred in outcome measures between baseline and end time-points were used to evaluate differences between control and intervention groups. Based on guidelines in the Cochrane Handbook, if the SD not available, we used a conservative within-subject pretest/post-test correlation value of 0.5 to calculate the SD of the change in each group [20]. Weighted mean differences were used to calculate changes in the HRQoL scores. The chi-square and I^2 tests were used to measure statistical heterogeneity [20]. When I^2 was <50% and p was >0.1, a fixed effect model was applied; otherwise, a random effect model was used [21]. The potential for publication bias was examined using funnel plots [22].

A subgroup analysis was performed using the same statistical methods for each of the following categories of physical activity: short-term (≤12 weeks); physical activity vs. medium-term (13–26 weeks); physical activity vs. long-term (>26 weeks) physical activity [23]; combined exercise vs. single exercise.

3. Results

3.1. *Trial flow and study characteristics*

Our literature search generated 450 relevant citations; among which, 407 were excluded on the basis of duplication, title, and

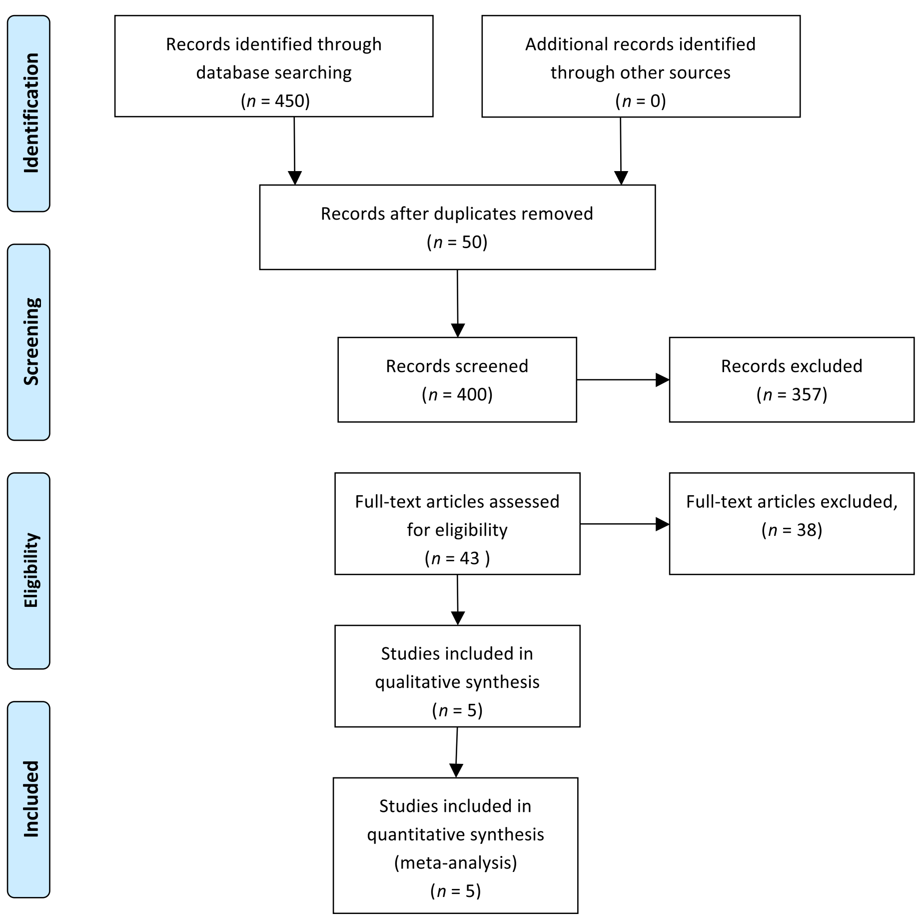


Fig. 1 – Flowchart of the trial selection process.

Table 1 – Characteristics of included randomized controlled trials.

Study (author/year)	Fracture history	Diagnostic criteria	Length of exercise	Type of exercise	Intervention group (regimen)	Control group (regimen)	Main outcomes
Bergland et al. (2011) [24]	Vertebral fracture	WHO criteria for osteoporosis and osteopenia	48 weeks	Combined exercise	(A) Warm up, balance training, posture promoting. stretch the muscles of the upper and lower limbs, n = 48	(B) No restrictions were placed on exercise activities, n = 47	QUALEFFO
Carter (2002) [25]	n.r.	WHO criteria for osteoporosis and osteopenia	20 weeks	Combined exercise	(A) Osteofit program: posture promoting, balance training, coordination, strengthening and stretching exercises and hip stabilization, n = 40	(B) Continue the routine daily activities, n = 40	QUALEFFO
Liu-Ambrose-1 (2005) [26]	n.r.	WHO criteria for osteoporosis and osteopenia	25 weeks	Single exercise	(A) muscle strength in the extremities (upper and lower) and trunk, n = 32	(B) Stretching (sham exercise), n = 32	QUALEFFO
Liu-Ambrose-2 (2005) [26]	n.r.	WHO criteria for osteoporosis and osteopenia	25 weeks	Single exercise	(A) balance training, coordination, and psychomotor performance, n = 34	(B) Stretching (sham exercise), n = 32	QUALEFFO
Nurten et al. (2013) [27]	without history of fracture	WHO criteria for osteoporosis and osteopenia	48 weeks	Combined exercise	(A) Pilates exercise program: postural education, maintaining neutral position, sitting exercises, antalgic exercises, stretching exercises, proprioceptive training, and respiratory training, n = 35	(B) Home exercises: thoracic extension exercises in the sitting position, n = 32	QUALEFO
Tuzun et al. (2010) [28]	n.r.	WHO criteria for osteoporosis and osteopenia	12 weeks	Single exercise	(A) Hatha yoga, n = 13	(B) Classic osteoporosis exercise: usual exercises, n = 13	QUALEFFO

n.r. not reported; QUALEFFO, Quality of Life Questionnaire of the European Foundation for Osteoporosis; WHO, World Health Organization.

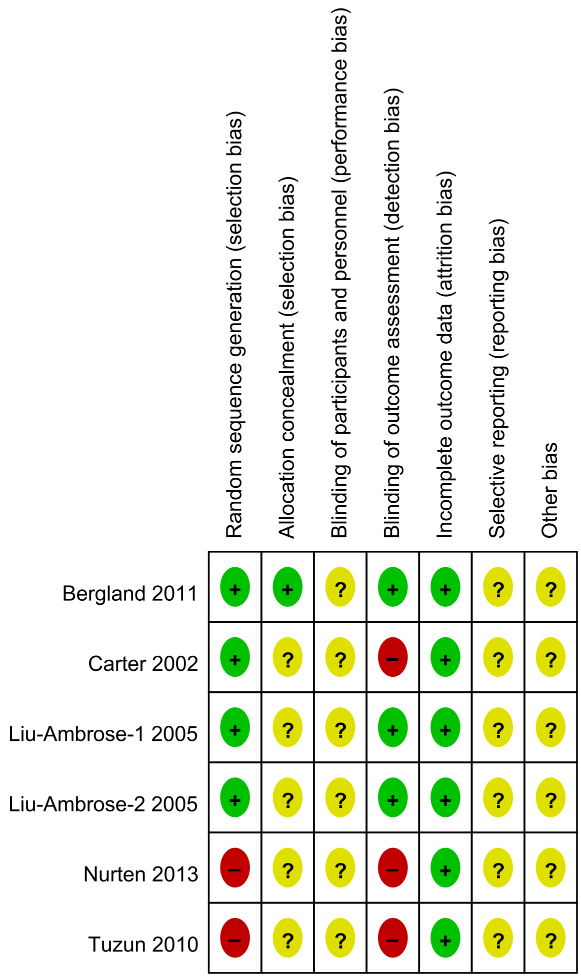


Fig. 2 – Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

abstract. Among the 43 remaining citations, 38 were excluded based on inclusion criteria. Finally, a total of five RCTs [24–28] involving 398 participants were deemed eligible and included in our final meta-analysis. However, the study conducted by Liu Ambrose [26] included two exercise groups, and thus data obtained from six trials were included in our analysis. A flowchart depicting the trial selection process is shown in Fig. 1. All patients in the included trials satisfied WHO criteria for osteoporosis and osteopenia. Except for one trial [27] which included subjects with either osteoporosis or osteopenia but without a fracture, no trial [24] in our analysis mentioned the fracture history of the participants. The intervention groups received either combined exercise [24,25,27] or single exercise [26,28], and the lengths of the exercise periods varied. One study [28] was conducted for 12 weeks (short-term), two studies [25,26] were conducted for 13–26 weeks (medium-term), and two other studies [24,27] were conducted for >26 weeks (long-term). Details regarding the five including RCTs included in our meta-analysis [24–28] are summarized in the Table 1.

3.2. *Risk of bias*

The Cochrane risk of bias results are presented in Figs. 2 and 3. Most trials had a small sample size. Three of the included RCTs [24–26] reported the sequence generation methods used for randomization; however, that information was not available for the remaining trials [27,28]. One RCT [24] used sealed envelopes to conceal patient allocation, while the others did not report such information. None of the trials employed patient blinding, and individuals who served as assessors were blinded in only two RCTs [24,26]. All of the included RCTs [24–28] mentioned the risk of dropout bias.

3.3. *Quantitative data synthesis*

3.3.1. *HRQoL in five domains*

Study participants in physical exercise groups showed significantly greater improvements in the physical function [N = 391, WMD = −3.22; 95% CI (−5.17, −1.28), $p = 0.001$] and pain [N = 391, WMD = −7.24; 95% CI (−12.73, −1.75), $p = 0.01$] domains of HRQoL compared to participants in the control groups (Fig. 4). Although data obtained from 391 participants showed that physical activity had insignificant effects on

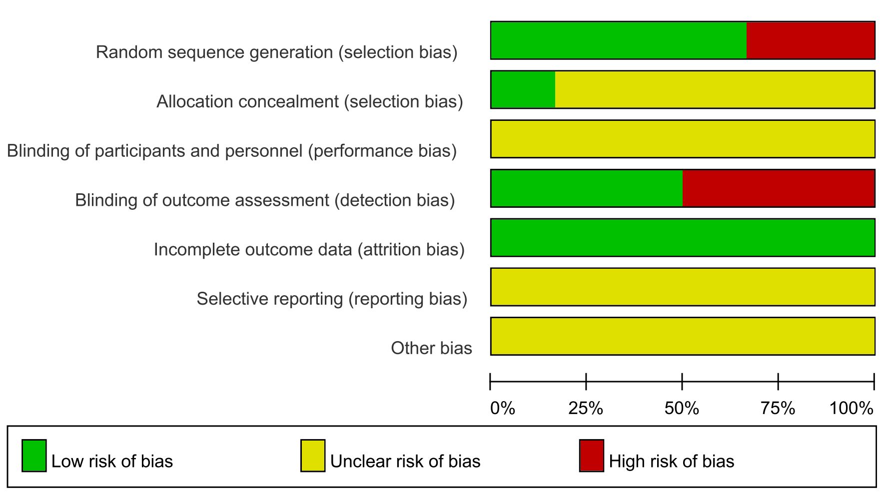
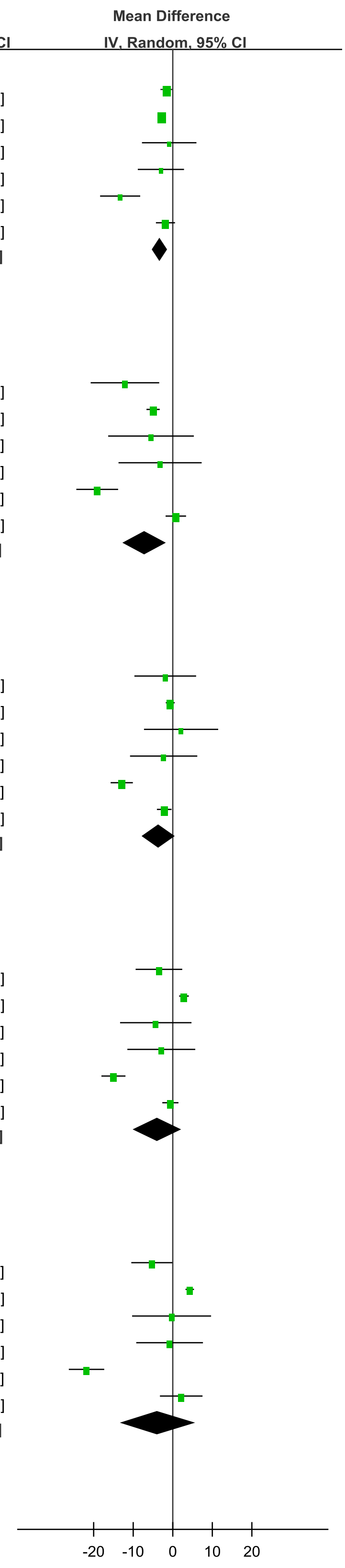


Fig. 3 – Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
1.1.1 physical function								
Bergland 2011	-2.5	4.97	48	-1	1.46	47	25.2%	-1.50 [-2.97, -0.03]
Carter 2002	-0.76	1.9	40	1.99	0.6	40	28.6%	-2.75 [-3.37, -2.13]
Liu-Ambrose-1 2005	-1.9	15.3	32	-1	12	32	6.5%	-0.90 [-7.64, 5.84]
Liu-Ambrose-2 2005	-4	11.5	34	-1	12	32	8.4%	-3.00 [-8.68, 2.68]
Nurten 2013	-16.8	9.3	30	-3.5	10.1	30	10.2%	-13.30 [-18.21, -8.39]
Tuzun 2010	-3.31	3.03	13	-1.46	2.83	13	21.1%	-1.85 [-4.10, 0.40]
Subtotal (95% CI)			**197**			**194**	**100.0%**	**-3.22 [-5.17, -1.28]**
Heterogeneity: Tau² = 3.34; Chi² = 21.27, df = 5 (*p* = 0.0007); I² = 76%								
Test for overall effect: Z = 3.25 (*p* = 0.001)								
1.1.2 pain								
Bergland 2011	-13.9	30	48	-1.8	2	47	14.4%	-12.10 [-20.61, -3.59]
Carter 2002	-6.55	4.8	40	-1.58	0.9	40	21.7%	-4.97 [-6.48, -3.46]
Liu-Ambrose-1 2005	-10.8	23.4	32	-5.3	20	32	12.0%	-5.50 [-16.17, 5.17]
Liu-Ambrose-2 2005	-8.5	22.9	34	-5.3	20	32	12.3%	-3.20 [-13.56, 7.16]
Nurten 2013	-23.4	11.3	30	-4.3	8.8	30	18.5%	-19.10 [-24.23, -13.97]
Tuzun 2010	-2.53	2.81	13	-3.3	3.47	13	21.1%	0.77 [-1.66, 3.20]
Subtotal (95% CI)			**197**			**194**	**100.0%**	**-7.24 [-12.73, -1.75]**
Heterogeneity: Tau² = 35.64; Chi² = 52.81, df = 5 (*p* < 0.00001); I² = 91%								
Test for overall effect: Z = 2.59 (*p* = 0.010)								
1.1.3 general health								
Bergland 2011	-1.7	19	48	0.2	19	47	13.1%	-1.90 [-9.54, 5.74]
Carter 2002	3.12	3	40	3.76	0.9	40	21.9%	-0.64 [-1.61, 0.33]
Liu-Ambrose-1 2005	0.3	22	32	-1.8	15	32	11.0%	2.10 [-7.13, 11.33]
Liu-Ambrose-2 2005	-4.1	19.5	34	-1.8	14.9	32	12.1%	-2.30 [-10.64, 6.04]
Nurten 2013	-14.1	6.6	30	-1.2	3.4	30	20.4%	-12.90 [-15.56, -10.24]
Tuzun 2010	-2.62	2.4	13	-0.46	1.97	13	21.4%	-2.16 [-3.85, -0.47]
Subtotal (95% CI)			**197**			**194**	**100.0%**	**-3.53 [-7.86, 0.80]**
Heterogeneity: Tau² = 22.06; Chi² = 72.98, df = 5 (*p* < 0.00001); I² = 93%								
Test for overall effect: Z = 1.60 (*p* = 0.11)								
1.1.4 social								
Bergland 2011	-3.3	15	48	0.2	13.5	47	16.3%	-3.50 [-9.24, 2.24]
Carter 2002	-0.32	3.42	40	-3.15	0.5	40	19.1%	2.83 [1.76, 3.90]
Liu-Ambrose-1 2005	-5.6	20	32	-1.3	16	32	13.5%	-4.30 [-13.17, 4.57]
Liu-Ambrose-2 2005	-4.2	18.8	34	-1.3	16.1	32	13.9%	-2.90 [-11.33, 5.53]
Nurten 2013	-16.7	6.6	30	-1.7	4.6	30	18.4%	-15.00 [-17.88, -12.12]
Tuzun 2010	-1.76	2.52	13	-1.15	2.39	13	18.8%	-0.61 [-2.50, 1.28]
Subtotal (95% CI)			**197**			**194**	**100.0%**	**-3.89 [-9.89, 2.11]**
Heterogeneity: Tau² = 48.86; Chi² = 134.07, df = 5 (*p* < 0.00001); I² = 96%								
Test for overall effect: Z = 1.27 (*p* = 0.20)								
1.1.5 mental health								
Bergland 2011	-2.6	12	48	2.7	13	47	17.1%	-5.30 [-10.33, -0.27]
Carter 2002	2.09	2.9	40	-2.2	0.5	40	17.9%	4.29 [3.38, 5.20]
Liu-Ambrose-1 2005	1.3	20.1	32	1.6	20	32	15.0%	-0.30 [-10.12, 9.52]
Liu-Ambrose-2 2005	0.8	14.9	34	1.6	19	32	15.7%	-0.80 [-9.07, 7.47]
Nurten 2013	-26.5	11	30	-4.7	4.9	30	17.3%	-21.80 [-26.11, -17.49]
Tuzun 2010	2.53	3.96	13	0.39	8.75	13	17.0%	2.14 [-3.08, 7.36]
Subtotal (95% CI)			**197**			**194**	**100.0%**	**-3.71 [-13.11, 5.68]**
Heterogeneity: Tau² = 128.06; Chi² = 146.57, df = 5 (*p* < 0.00001); I² = 97%								
Test for overall effect: Z = 0.77 (*p* = 0.44)								



Test for subgroup differences: Chi² = 1.84, df = 4 (*p* = 0.77), I² = 0%

Fig. 4 – Meta analysis on health-related quality of life in five dominates.

scores in the social [WMD = −3.89; 95% CI (−9.89, 2.11), $p = 0.20$] and mental health [WMD = −3.71; 95% CI (−13.11, 5.68), $p = 0.44$] domains of HRQoL, a favorable trend in the general health component score was observed [WMD = −3.53; 95% CI (−7.86, 0.80), $p = 0.11$] (Fig. 4).

3.3.2. *Short-term vs. medium-term vs. long-term physical therapy*

Although one study in our analysis included participant follow-up periods in the category of short-term exercise [28], the results of our meta-analysis showed that when compared to participants in control groups, participants in short-term physical activity groups had significantly better results in the general health domains of the HRQoL [N = 13, WMD = −2.16; 95% CI (−3.85, −0.47), $p = 0.01$] (Fig. 5). Moreover, although two RCTs [25,26] included their follow-up periods in the category of middle-term exercise, our meta-analysis showed that compared with participants in control groups, participants in middle-term exercise groups had significantly better results on the physical function [N = 208, WMD = −2.74; 95% CI (−3.35, −2.13), $p < 0.01$], and pain [N = 208, WMD = −4.95; 95% CI (−6.43, −3.46), $p < 0.01$] domains of the HRQoL questionnaire (Fig. 6). Two RCTs [24,27] which investigated the long-term effects of physical exercise reported that subjects who participated in physical activity had significantly better scores in the pain domains of the HRQoL [N = 155, WMD = −3.22; 95% CI (−23.11, −9.81), $p < 0.01$] when compared with subjects in control groups (Fig. 7).

3.3.3. *Combined exercise vs. single exercise*

Three RCTs [24,25,27] examined the effects combined exercise, and our meta-analysis showed that compared with subjects in control groups, subjects in combined exercise groups showed significant improvements in the physical function [N = 235, WMD = −4.37; 95% CI (−7.39, −1.36), $p = 0.0004$], and pain [N = 235, WMD = −11.85; 95% CI (−22.06, −1.65), $p = 0.02$] domains of HRQoL (Fig. 8). However, subjects in single exercise groups had physical function and pain scores similar to those recorded for subjects in control groups [26,28] (Fig. 9).

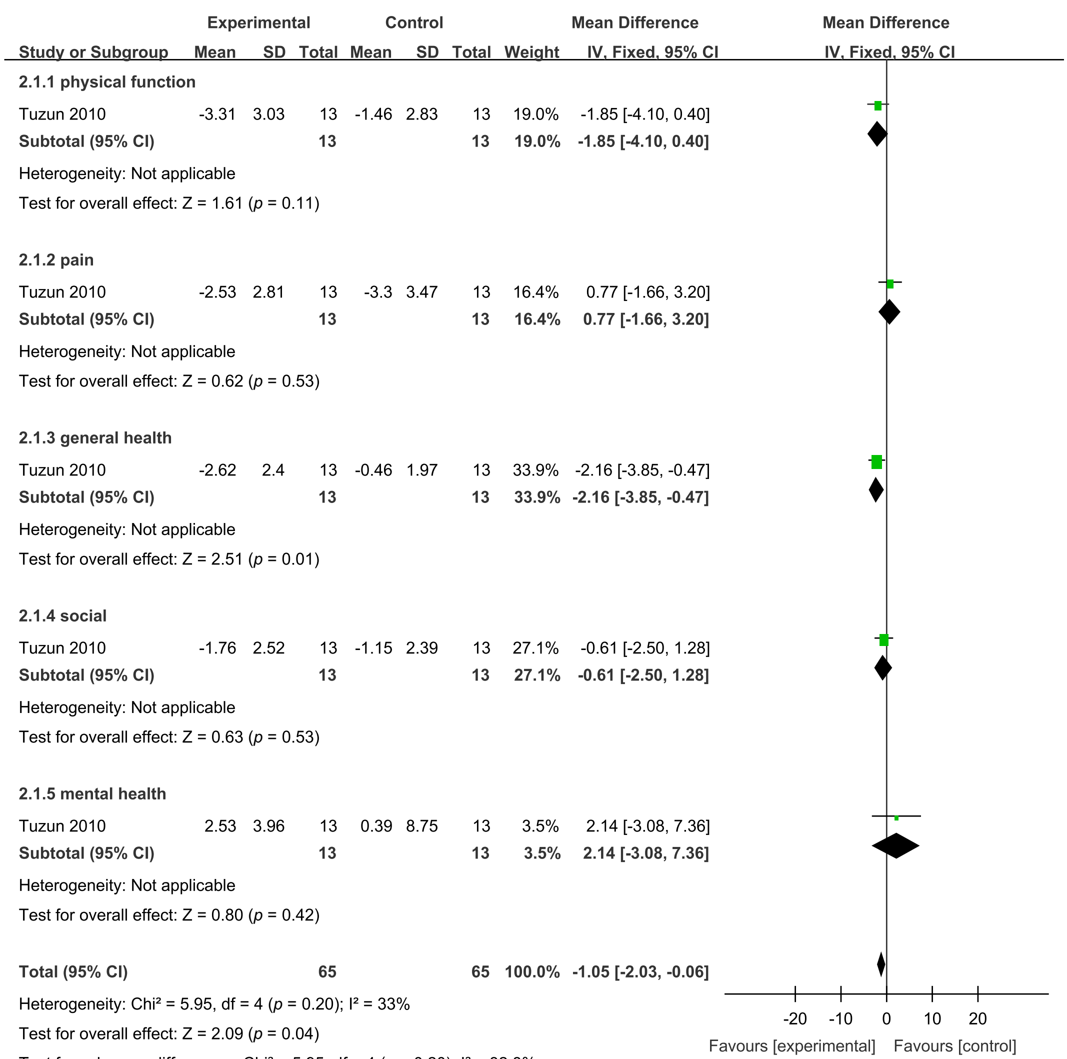
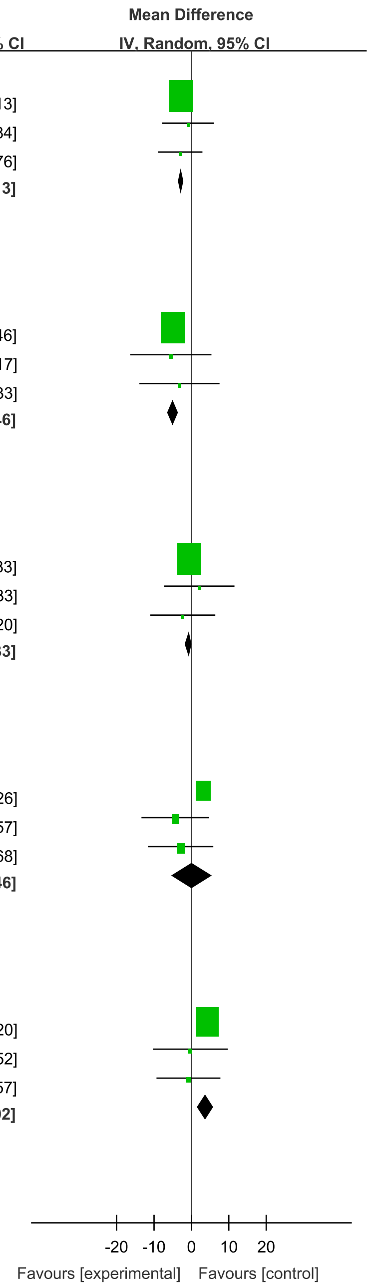


Fig. 5 – Short-term physical therapy on health-related quality of life in five dominates.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 physical function								
Carter 2002	-0.76	1.9	40	1.99	0.6	40	98.0%	-2.75 [-3.37, -2.13]
Liu-Ambrose-1 2005	-1.9	15.3	32	-1	12	32	0.8%	-0.90 [-7.64, 5.84]
Liu-Ambrose-2 2005	-4	11.5	32	-1	12	32	1.1%	-3.00 [-8.76, 2.76]
Subtotal (95% CI)			**104**			**104**	**100.0%**	**-2.74 [-3.35, -2.13]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.30$, df = 2 ($p = 0.86$); $I^2 = 0\%$								
Test for overall effect: Z = 8.78 ($p < 0.00001$)								
2.2.2 pain								
Carter 2002	-6.55	4.8	40	-1.58	0.9	40	96.1%	-4.97 [-6.48, -3.46]
Liu-Ambrose-1 2005	-10.8	23.4	32	-5.3	20	32	1.9%	-5.50 [-16.17, 5.17]
Liu-Ambrose-2 2005	-8.5	22.9	32	-5.3	20	32	2.0%	-3.20 [-13.73, 7.33]
Subtotal (95% CI)			**104**			**104**	**100.0%**	**-4.95 [-6.43, -3.46]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.12$, df = 2 ($p = 0.94$); $I^2 = 0\%$								
Test for overall effect: Z = 6.53 ($p < 0.00001$)								
2.2.3 general health								
Carter 2002	3.12	3	40	3.76	0.9	40	97.6%	-0.64 [-1.61, 0.33]
Liu-Ambrose-1 2005	0.3	22	32	-1.8	15	32	1.1%	2.10 [-7.13, 11.33]
Liu-Ambrose-2 2005	-4.1	19.5	32	-1.8	14.9	32	1.3%	-2.30 [-10.80, 6.20]
Subtotal (95% CI)			**104**			**104**	**100.0%**	**-0.63 [-1.59, 0.33]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.48$, df = 2 ($p = 0.78$); $I^2 = 0\%$								
Test for overall effect: Z = 1.29 ($p = 0.20$)								
2.2.4 social								
Carter 2002	-0.32	3.42	40	-3.51	0.5	40	55.4%	3.19 [2.12, 4.26]
Liu-Ambrose-1 2005	-5.6	20	32	-1.3	16	32	21.8%	-4.30 [-13.17, 4.57]
Liu-Ambrose-2 2005	-4.2	18.8	32	-1.3	16.1	32	22.8%	-2.90 [-11.48, 5.68]
Subtotal (95% CI)			**104**			**104**	**100.0%**	**0.17 [-5.12, 5.46]**
Heterogeneity: $Tau^2 = 12.85$; $Chi^2 = 4.54$, df = 2 ($p = 0.10$); $I^2 = 56\%$								
Test for overall effect: Z = 0.06 ($p = 0.95$)								
2.2.5 mental health								
Carter 2002	2.09	2.9	40	-2.2	0.5	40	89.1%	4.29 [3.38, 5.20]
Liu-Ambrose-1 2005	1.3	20.1	32	1.6	20	32	4.6%	-0.30 [-10.12, 9.52]
Liu-Ambrose-2 2005	0.8	14.9	32	1.6	19	32	6.3%	-0.80 [-9.17, 7.57]
Subtotal (95% CI)			**104**			**104**	**100.0%**	**3.76 [1.59, 5.92]**
Heterogeneity: $Tau^2 = 1.15$; $Chi^2 = 2.22$, df = 2 ($p = 0.33$); $I^2 = 10\%$								
Test for overall effect: Z = 3.40 ($p = 0.0007$)								



Test for subgroup differences: $Chi^2 = 56.11$, df = 4 ($p < 0.00001$), $I^2 = 92.9\%$

Fig. 6 – Medium-term physical therapy on health-related quality of life in five dominates.

3.3.4. *Adverse events*

None of the five included RCTs reported any adverse effects resulting from physical therapy.

3.4. *Publication bias*

The potential for publication bias was examined using the funnel plot method, and results showed evidence for publication bias in our systematic review (Fig. 10).

3.5. *Sensitivity analysis*

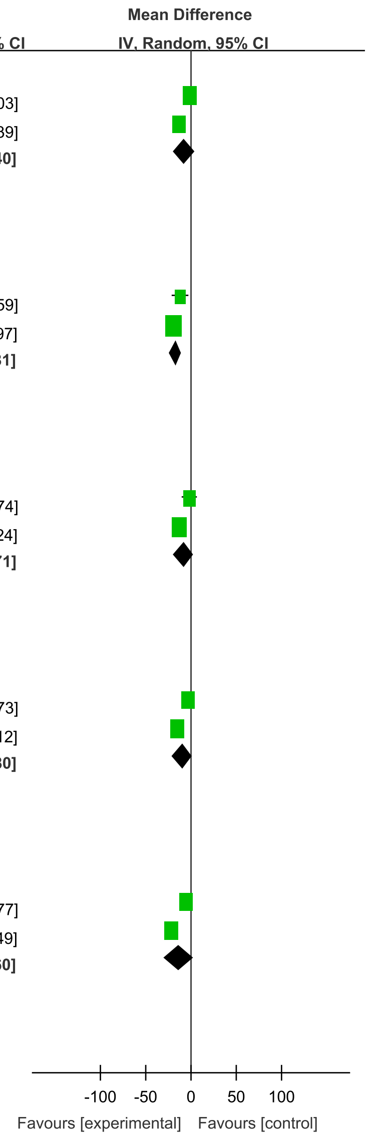
A sensitivity analysis was performed to assess the influence of each individual study on the pooled meta-analysis results. When omitting the heterogeneity contributed by Nurten's study [27], our pooled results were consistent with those in the previous analysis; suggesting the stability of results in our current meta-analysis.

4. Discussion

4.1. *Physical activity had beneficial effects on the HRQoL of postmenopausal women with osteoporosis or osteopenia*

The results of our meta-analyses suggest that participation in physical activity has beneficial effects on the HRQoL of osteoporotic and osteopenic postmenopausal women. More

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.3.1 physical function								
Bergland 2011	-2.5	4.97	48	-1	1.46	47	52.1%	-1.50 [-2.97, -0.03]
Nurten 2013	-16.8	9.3	30	-3.5	10.1	30	47.9%	-13.30 [-18.21, -8.39]
Subtotal (95% CI)			**78**			**77**	**100.0%**	**-7.16 [-18.71, 4.40]**
Heterogeneity: Tau² = 66.20; Chi² = 20.35, df = 1 (p < 0.00001); I² = 95%								
Test for overall effect: Z = 1.21 (p = 0.22)								
2.3.2 pain								
Bergland 2011	-13.9	30	48	-1.8	2	47	37.8%	-12.10 [-20.61, -3.59]
Nurten 2013	-23.4	11.3	30	-4.3	8.8	30	62.2%	-19.10 [-24.23, -13.97]
Subtotal (95% CI)			**78**			**77**	**100.0%**	**-16.46 [-23.11, -9.81]**
Heterogeneity: Tau² = 11.66; Chi² = 1.91, df = 1 (p = 0.17); I² = 48%								
Test for overall effect: Z = 4.85 (p < 0.00001)								
2.3.3 general health								
Bergland 2011	-1.7	19	48	0.2	19	47	44.5%	-1.90 [-9.54, 5.74]
Nurten 2013	-14.1	6.6	30	-1.2	3.4	30	55.5%	-12.90 [-15.56, -10.24]
Subtotal (95% CI)			**78**			**77**	**100.0%**	**-8.01 [-18.72, 2.71]**
Heterogeneity: Tau² = 51.98; Chi² = 7.10, df = 1 (p = 0.008); I² = 86%								
Test for overall effect: Z = 1.46 (p = 0.14)								
2.3.4 social								
Bergland 2011	-3.3	12.5	48	0.2	13.5	47	48.1%	-3.50 [-8.73, 1.73]
Nurten 2013	-16.7	6.6	30	-1.7	4.6	30	51.9%	-15.00 [-17.88, -12.12]
Subtotal (95% CI)			**78**			**77**	**100.0%**	**-9.47 [-20.73, 1.80]**
Heterogeneity: Tau² = 61.48; Chi² = 14.24, df = 1 (p = 0.0002); I² = 93%								
Test for overall effect: Z = 1.65 (p = 0.10)								
2.3.5 mental health								
Bergland 2011	-2.6	9.14	48	2.7	13	47	49.9%	-5.30 [-9.83, -0.77]
Nurten 2013	-26.5	11	30	-4.7	4.9	30	50.1%	-21.80 [-26.11, -17.49]
Subtotal (95% CI)			**78**			**77**	**100.0%**	**-13.57 [-29.73, 2.60]**
Heterogeneity: Tau² = 131.04; Chi² = 26.77, df = 1 (p < 0.00001); I² = 96%								
Test for overall effect: Z = 1.64 (p = 0.10)								



Test for subgroup differences: Chi² = 3.14, df = 4 (p = 0.53), I² = 0%

Fig. 7 – Long-term physical therapy on health-related quality of life in five dominates.

specifically, physical activity appeared to improve scores in the subjective physical functioning and pain components of the QUALEFFO questionnaire. A subgroup analysis showed greater improvements in physical function and pain scores for subjects in the combined exercise and medium to long-term exercise groups. Furthermore, scores for general health showed significantly greater improvement in the short-term exercise group. Patients in both the experimental and control groups participated in physical activity programs recommended by the American College of Sports Medicine, and the programs were supervised by physiotherapists throughout the course of each clinical trial. However, rather than only performing routine daily activities, most subjects in the experimental groups participated in group-based exercise programs; thus their quality of life may have benefitted from the increased social interactions, when compared with control subjects.

4.2. *The current meta-analysis compared to a past meta-analysis*

In 1999, Li et al. [15] performed a meta-analysis of 4 RCTs for the purpose of examining the effects of exercise on quality of life in postmenopausal women with osteoporosis or osteopenia, and those results showed greater improvements in physical function and pain among subjects in physical activity groups. The results of our current study mostly agree with those in the previous study, and indicate that osteoporotic and osteopenic postmenopausal women can benefit from participating in supervised physical activity. Nevertheless, our subgroup analysis showed that short-time exercise produced no statistically significant changes in HRQoL except for the general health domain, and this result appears to be inconsistent with that reported by Li et al. [15]. Our meta-analysis included the results from recent RCTs (published

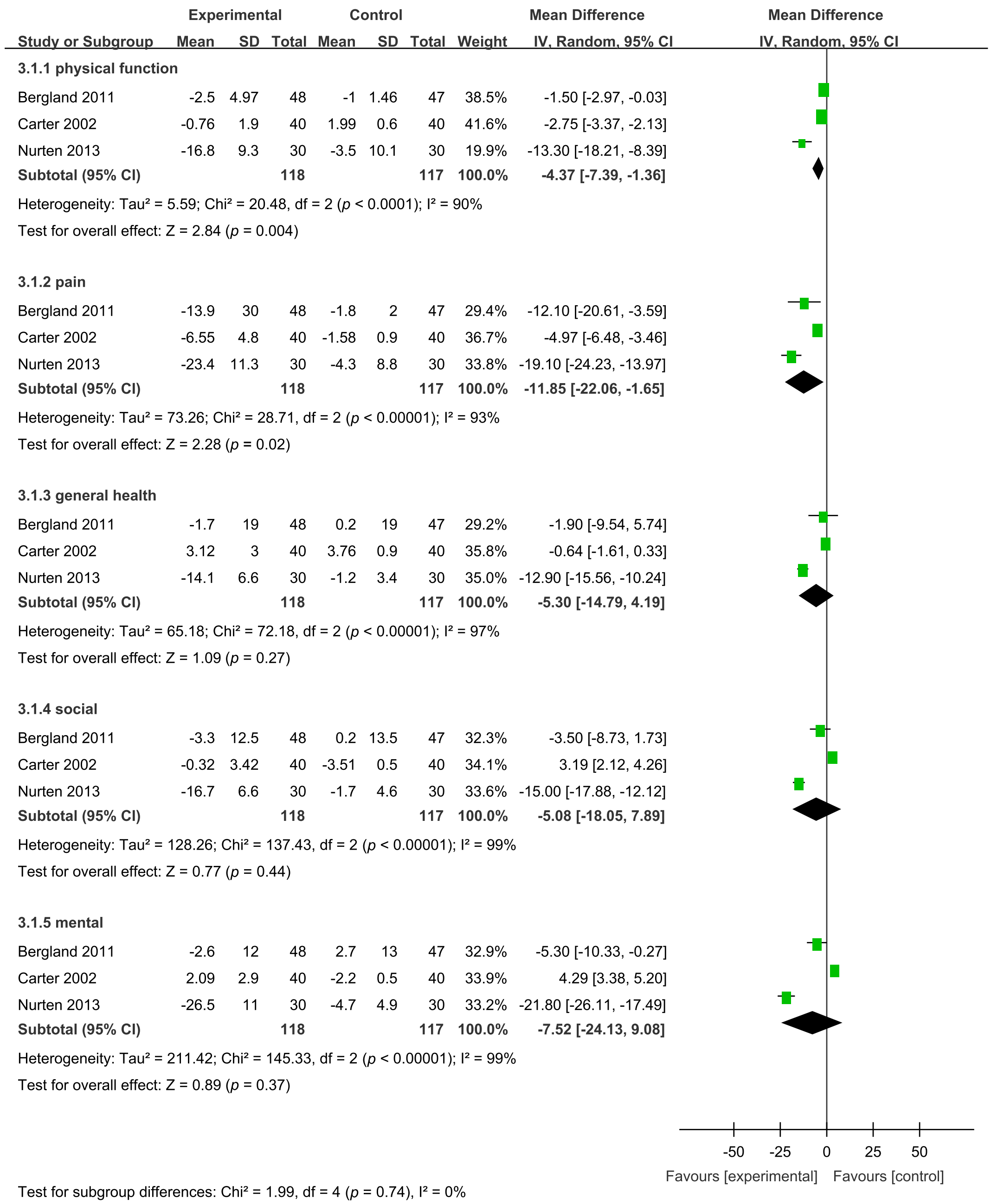


Fig. 8 – Combined exercise physical therapy on health-related quality of life in five dominates.

after 2009) which examined the effects of physical activity, and it is important to realize that any meta-analysis should be periodically updated as results for additional RCTs are published. Moreover, two studies included in the previous analysis utilized the generic SF-36 questionnaire to measure patient outcomes. The SF-36 is a generic instrument that often contains superfluous questions, and these types of questionnaires are less accurate when used to detect changes in specific subpopulations [13,16]. Hence, conclusions reached in studies which used a generic instrument to measure quality of life should be viewed with caution. Recent evidence suggests that short-term improvements in general health resulting from physical activity actually stimulate an individual to engage in further activities or social events which improve physical function and relieve pain in the long term.

4.3. *Methodological quality*

The methodological quality of each study was evaluated using the risk of bias assessment tool described in the Cochrane Handbook. Only 17% of the RCTs in our comprehensive review reported adequate random allocation and allocation concealment methods. Results from trials with inadequate random allocation concealment methods are subject to selection bias, and thus more likely to overestimate the results shown by their outcome measures [29,30]. Finally, exercise interventions are difficult to conduct in a blinded manner; and

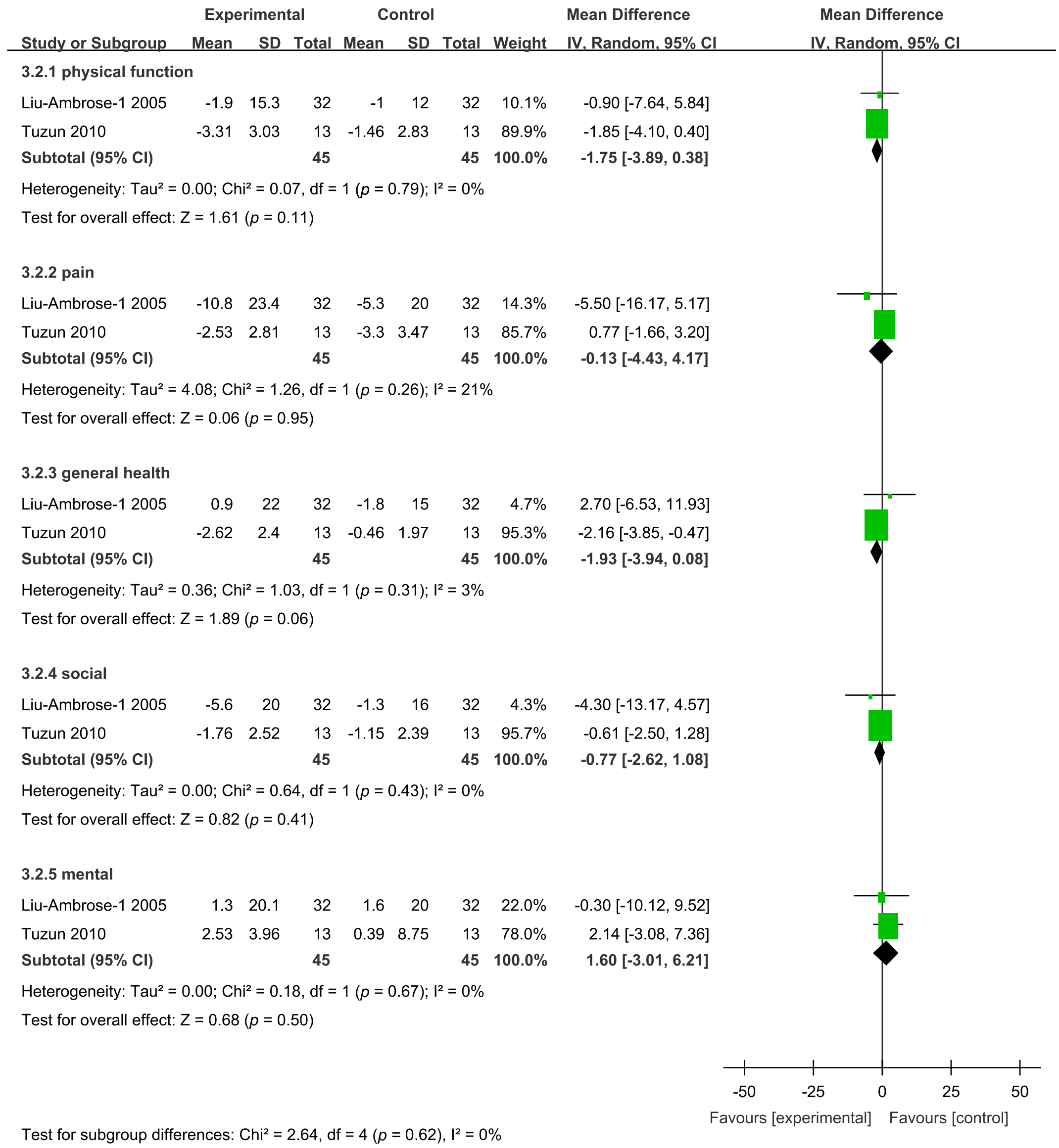


Fig. 9 — Single exercise physical therapy on health-related quality of life in five dominates.

furthermore, only 50% of the included studies mentioned the use of blinded assessors. As a result, caution must be taken when attempting to generalize the results of our analysis due to the overall low quality of the included studies.

The inclusion of a placebo or sham exercise group that can be compared with an actual exercise group may be crucial when conducting an RCT measuring the effects of exercise. While studies included in the analysis performed by Liu-Ambrose [26] used a sham exercise in the control group, a strong placebo effect is often found when measuring pain [31,32], and thus results which show improvements in pain continue to be controversial.

4.4. *QUALEFFO questionnaire*

The osteoporosis-specific quality of life questionnaire was published in the English language [18,19], and thus when using it in global clinical practice, researchers should be certain that the concepts tested apply to all cultures and are understood in all languages. Indeed, numerous questionnaires published in languages other than English have already been used in many countries, including Serbia [33], Spain [34], Iran [35], and Portugal [36]. In the future, the QUALEFFO questionnaire must be proven to be reliable and valuable tool when used for gathering quality of life information in China and from people with a Chinese cultural background.

4.5. *Adverse events*

No major exercise-related adverse event was reported in the studies included in our meta-analysis, and the exercise adherence rates ranged from 80% to 100%. While some participants were lost to follow-up, dropped out or discontinued participation in physical activity due to hospitalization or death, no subject stopped participating in a trial due to an exercise-related adverse event. Thus there is insufficient evidence to verify that it is not safe for postmenopausal

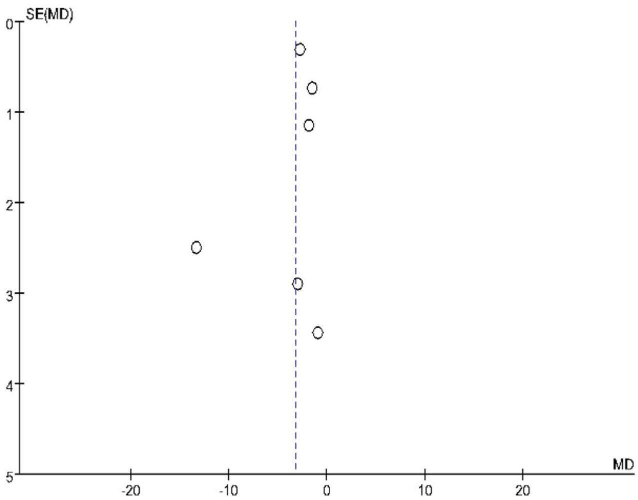


Fig. 10 – Funnel plot of publication bias.

osteoporotic or osteopenic women to participate in organized physical activity.

4.6. *Limitations*

Our meta-analysis has several important limitations that should be mentioned. First, the analysis included a small number of RTCs, each of which had a small sample size; thus caution must be used when generalizing its results. While there are no rules regarding sample-size requirements for a meta-analysis, the results of a meta-analysis can be overestimated due to an insufficient number of patients [37]. Therefore, larger numbers of patients should be included in future studies. Second, bone fracture is an important consequence of osteoporosis and can affect an individual's quality of life [38]. However, only one RCT in our analysis mentioned a history of bone fracture [24]. Third, our meta-analysis showed evidence of publication bias.

5. Conclusions

Overall, as a relatively safe alternative to pharmacologic intervention, our results suggest that physical activity has a beneficial effect on HRQoL in osteoporotic and osteopenic postmenopausal women, and especially in the physical and pain domains of HRQoL. Compared to activity provided by a single exercise, activity provided by combined exercise showed a more favorable effect on physical function and pain. Additionally, different durations of exercise produced improvement in different domains. In the future, results from RCTs with more rigorous standards must be obtained to overcome the limitations of our existing data, and reach more reliable conclusions.

Conflict of interest

The authors have no conflicts of interest to declare. Additionally, they have no affiliation with or involvement in any organization or entity with a financial interest concerning the subject matter of the study.

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Appendix A. Search strategies

MEDLINE

1 postmenopause/
2 (post menopaus$ or postmenopaus$ or post-menopaus$).tw.
3 1 or 2
4 exp osteoporosis/
5 bone loss$.tw.
6 osteoporos#s.tw.
7 bone density/
8 (bone adj2 (density or fragil$)).tw.
9 bone mass.tw.
10 exp Fracture/
11 fracture$.tw.
12 or/4-11
13. exp EXERCISE/
14. exp exertion/
15. exp Physical Fitness/
16. exp Exercise Test/
17. exp Exercise Tolerance/
18. exp Sports/
19. exp PLIABILITY/
20. exp Physical Endurance/
21. exertion$.tw.
22. exercis$.tw.
23. sport$.tw.
24. ((physical or motion) adj5 (fitness or therap$)).tw.
25. (physical$ adj2 endur$).tw.
26. ((strength$ or isometric$ or isotonic$ or isokinetic$ or aerobic$ or endurance or weight$) adj5 (exercis$ or train$)).tw.
27. exp physical therapy modalities/
28. physiotherap$.tw.
29. manipulat$.tw.
30. kinesiotherap$.tw.
31. exp Rehabilitation/
32. rehab$.tw.
33. (skate$ or skating).tw.
34. run$.tw.
35. jog$.tw.
36. treadmill$.tw.
37. swim$.tw.
38. bicycl$.tw.
39. (cycle$ or cycling).tw.
40. walk$.tw.
41. (row or rows or rowing).tw.
42. muscle strength$.tw.
43. or/13-43

44. "quality of life"/
45. exp health status/
46. "activities of daily living"/
47. life qualit$.mp.
48. exp self concept/
49. health level.mp.
50. level of health.mp.
51. wellness.mp.
52. well being.mp.
53. or/44-52
54. randomized.ab.
55. placebo.ab.
56. randomly.ab.
57. trial.ab.
58. randomized controlled trial.pt.
59. controlled clinical trial.pt.
60. random$.ab
61. 54 or 55 or 56 or 57 or 58 or 59 or 60
62 3 and 12 and 43 and 53 and 61

Appendix B. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ijnss.2015.04.002.

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